

REMARKS

Claim Amendments

Claims 1-40 were pending. Claims 1, 7-11, 14 and 38 have been amended and claims 2-6, 12-13 and 15-34 have been canceled. Accordingly, Claims 1, 7-11, 14 and 35-38 remain pending.

No new matter has been added by way of the foregoing amendment, which has been made solely to expedite prosecution and in no way should be viewed as acquiescence to any rejection. Applicants reserve the right to pursue the claims as originally filed in this or subsequent applications.

Restriction Requirement

The Examiner has required restriction between the following inventions in the above-identified application:

Group 1: Claims 1-4, 7-8, drawn to a mouse MEKK1 protein or fragment thereof, which MEKK1 mediates apoptosis, classified in class 530, subclass 350;

Group 2: Claims 1-3, 5, 8, 39-40, drawn to a human MEKK1 protein or fragment thereof, which MEKK1 mediates apoptosis, or has kinase activity, classified in class 530, subclass 350;

Group 3: Claims 1-3, 6, 8, drawn to a rat MEKK1 protein or a fragment thereof, which MEKK1 mediates apoptosis, classified in class 530, subclass 350;

Group 4: Claims 9-14, drawn to a variant mouse MEKK1 protein or a fragment thereof, having substitutions, such that the MEKK1 is resistant to proteolysis, classified in class 530, subclass 350;

Group 5: Claims 9-13, 15, drawn to a variant human MEKK1 protein or a fragment thereof, having substitutions, such that the MEKK1 is resistant to proteolysis, classified in class 530, subclass 350;

Group 6: Claims 9-13, 16, a variant rat MEKK1 protein or a fragment thereof, having substitutions, such that the MEKK1 is resistant to proteolysis, classified in class 530, subclass 350;

Group 7: Claims 17-20, 23-24, 31, 33, drawn to a nucleic acid encoding a mouse MEKK1 protein or fragment thereof, which MEKK1 mediates apoptosis, classified in class 530, subclass 23.1;

Group 8: Claims 17-19, 21, 23-24, 31, 33, drawn to a nucleic acid encoding a human MEKK1 protein or fragment thereof, which MEKK1 mediates apoptosis, classified in class 530, subclass 23.1;

Group 9: Claims 17-19, 22-24, 31, 33, drawn to a nucleic acid encoding a rat MEKK1 protein or fragment thereof, which MEKK1 mediates apoptosis, classified in class 530, subclass 23.1;

Group 10: Claims 25-28, 32, 34, drawn to a nucleic acid encoding a variant mouse MEKK1 protein or fragment thereof, having substitutions, such that the MEKK1 is resistant to proteolysis, classified in class 530, subclass 23.1;

Group 11: Claims 25-27, 29, 32, 34, drawn to a nucleic acid encoding a variant human MEKK1 protein or fragment thereof, having substitutions, such that the MEKK1 is resistant to proteolysis, classified in class 530, subclass 23.1;

Group 12: Claims 25-27, 30, 32, 34, drawn to a nucleic acid encoding a variant rat MEKK1 protein or fragment thereof, having substitutions, such that the MEKK1 is resistant to proteolysis, classified in class 530, subclass 23.1;

Group 13: Claim 35, drawn to a method for stimulating apoptosis, using an expressing vector encoding a mouse MEKK1 active fragment, classified in class 514, subclass 44;

Group 14: Claim 35, drawn to a method for stimulating apoptosis, using an expressing vector encoding a human MEKK1 active fragment, classified in class 514, subclass 44;

Group 15: Claim 35, drawn to a method for stimulating apoptosis, using an expressing vector encoding a rat MEKK1 active fragment, classified in class 514, subclass 44;

Group 16: Claim 36, drawn to a method for inhibiting apoptosis, using a expressing vector encoding a mouse protease-resistant MEKK1 protein, classified in class 514, subclass 44;

Group 17: Claim 36, drawn to a method for inhibiting apoptosis, using a expressing vector encoding a human protease-resistant MEKK1 protein, classified in class 514, subclass 44;

Group 18: Claim 36, drawn to a method for inhibiting apoptosis, using a expressing vector encoding a rat protease-resistant MEKK1 protein, classified in class 514, subclass 44;

Group 19: Claim 37, drawn to a method for generating a mouse MEKK1 active fragment, classified in class 435, subclass 7.1;

Group 20: Claim 37, drawn to a method for generating a human MEKK1 active fragment, classified in class 435, subclass 7.1;

Group 21: Claim 37, drawn to a method for generating a rat MEKK1 active fragment, classified in class 435, subclass 7.1;

Group 22: Claim 38, drawn to a method for identifying a compound that modulates the apoptotic activity of a mouse active MEKK1 fragment, classified in class 435, subclass 7.1;

Group 23: Claim 38, drawn to a method for identifying a compound that modulates the apoptotic activity of a human active MEKK1 fragment, classified in class 435, subclass 7.1; and

Group 24: Claim 38, drawn to a method for identifying a compound that modulates the apoptotic activity of a rat active MEKK1 fragment, classified in class 435, subclass 7.1.

Accordingly, Applicants hereby elect, with traverse, Group 1 (claims 1-4 and 7-8) drawn to a mouse MEKK1 protein or fragment thereof, which MEKK1 mediates apoptosis, for continued examination.

Applicants respectfully traverse the restriction requirement with respect to Groups 1-3 and submit that since these groups are drawn to structurally similar subject matter, they should

be re-grouped as one single Group, *i.e.*, Group 1. Further, to clarify the structural similarity between these Groups, claim 1 has been amended to specify an isolated fragment having 95% identity to an amino acid sequence consisting of about amino acids 875-1493 of SEQ ID NO:3. Similarly, claim 8 has been amended to specify an isolated polypeptide comprising an amino acid sequence set forth in SEQ ID NO:3 or an amino acid sequence 95% identical thereto. As such, the subject matter of Groups 1-3 should properly be re-grouped as one single group.

Moreover, Applicants respectfully traverse the restriction requirement between linked Groups 1-3 and linked Groups 4-6. Applicants submit that Groups 4-6 should properly be included in Group 1 based on the common shared utility (*i.e.*, ability to mediate apoptosis) and the high degree of homology shared by the claimed proteins and corresponding variants. As evidenced by the enclosed sequence alignment (enclosed herewith as Appendix A), the full-length MEKK protein, the MEKK proteins containing mutations at residues 871-874 and the active fragment (comprising amino acids residues 875-1493) are highly homologous and therefore should be re-grouped with elected Group 1.

Applicants further note that, once the product claims are found allowable, the nonelected process claim (*e.g.*, Groups 22-24, *i.e.*, claim 38) will be rejoined in accordance with MPEP 821.04.

The Examiner has further required election of MEKK1.1 or MEKK1.2 as a species in the above-identified application. Accordingly, Applicants hereby elect the species of MEKK1 as set forth as SEQ ID NO:3 (previously referred to as "MEKK1.2") for continued examination. All of the pending claims, as amended to clarify the structural and functional relatedness of the claimed subject matter, read on the elected species. Further, Applicants respectfully submit that Applicants will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 C.F.R. § 1.141 *et seq.*

CONCLUSION

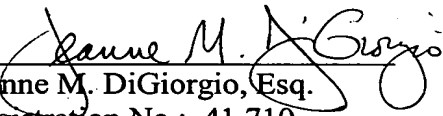
If the Examiner believes that a telephone conversation with Applicants' Attorney would be helpful in expediting prosecution of this application, the Examiner is invited to call the undersigned at (617) 227-7400.

The Director is hereby authorized to charge any deficiency in the fees filed, asserted to be filed or which should have been filed herewith (or with any paper hereafter filed in this application by this firm) to our Deposit Account No. 12-0080, under Order No. CPI-042CN2. A duplicate copy of this paper is enclosed.

In view of the above amendment, applicant believes the pending application is in condition for allowance.

Dated: March 12, 2007

Respectfully submitted,

By 
Jeanne M. DiGiorgio, Esq.

Registration No.: 41,710

For Debra J. Milasincic

Registration No.: 46,931

LAHIVE & COCKFIELD, LLP

One Post Office Square

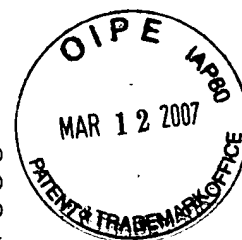
Boston, Massachusetts 02109-2127

(617) 227-7400

(617) 742-4214 (Fax)

Attorney/Agent For Applicant

Appendix A



CLUSTAL W (1.82) multiple sequence alignment

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MEKK      MAAAAGDRASSSGFPGAAAASPEAGGGGGGGGALQSGGAPAAGAAGLLREPGSAGRERAD
871      MAAAAGDRASSSGFPGAAAASPEAGGGGGGGGALQSGGAPAAGAAGLLREPGSAGRERAD
871-874   MAAAAGDRASSSGFPGAAAASPEAGGGGGGGGALQSGGAPAAGAAGLLREPGSAGRERAD
Active   -----

MEKK      WRRRQLRKVRSVELDQLPEQPLFLAAASPPCPSTSPSPPEPADAAGASRFQPAAGPPPPG
871      WRRRQLRKVRSVELDQLPEQPLFLAAASPPCPSTSPSPPEPADAAGASRFQPAAGPPPPG
871-874   WRRRQLRKVRSVELDQLPEQPLFLAAASPPCPSTSPSPPEPADAAGASRFQPAAGPPPPG
Active   -----

MEKK      AASRCGSHSAELAAARDSGARSPAGAEPPSAAAPSGREMENKETLKGLHKMEDRPEERMI
871      AASRCGSHSAELAAARDSGARSPAGAEPPSAAAPSGREMENKETLKGLHKMEDRPEERMI
871-874   AASRCGSHSAELAAARDSGARSPAGAEPPSAAAPSGREMENKETLKGLHKMEDRPEERMI
Active   -----

MEKK      REKLKATCMPAWKHEWLERRNRRGPVVVKPIPIKGDGSEVNNLAAEPQEGQAGSAAPAP
871      REKLKATCMPAWKHEWLERRNRRGPVVVKPIPIKGDGSEVNNLAAEPQEGQAGSAAPAP
871-874   REKLKATCMPAWKHEWLERRNRRGPVVVKPIPIKGDGSEVNNLAAEPQEGQAGSAAPAP
Active   -----

MEKK      KGRRSPSPGSSPSGRSVKPESPGVRRKRVSPVPFQSGRITPPRRAPSPDGFSPYSPEETS
871      KGRRSPSPGSSPSGRSVKPESPGVRRKRVSPVPFQSGRITPPRRAPSPDGFSPYSPEETS
871-874   KGRRSPSPGSSPSGRSVKPESPGVRRKRVSPVPFQSGRITPPRRAPSPDGFSPYSPEETS
Active   -----

MEKK      RRVNKMVRARLYLLQQIGPNSFLIGGSDPDNKYRVFIGPQNCSCGRGAFCIHLLFVMLRV
871      RRVNKMVRARLYLLQQIGPNSFLIGGSDPDNKYRVFIGPQNCSCGRGAFCIHLLFVMLRV
871-874   RRVNKMVRARLYLLQQIGPNSFLIGGSDPDNKYRVFIGPQNCSCGRGAFCIHLLFVMLRV
Active   -----

MEKK      FQLEPSDPLWRKTLKNFEVESLFQKYHSRRSSRIKAPSRNTIQKFVSRMSNSHTLSSSS
871      FQLEPSDPLWRKTLKNFEVESLFQKYHSRRSSRIKAPSRNTIQKFVSRMSNSHTLSSSS
871-874   FQLEPSDPLWRKTLKNFEVESLFQKYHSRRSSRIKAPSRNTIQKFVSRMSNSHTLSSSS
Active   -----

MEKK      TSTSSSENSIKDEEEQMCPICLLGMLDEESLTVCEDGCRNKLHHHCMSIWAEECRNRREP
871      TSTSSSENSIKDEEEQMCPICLLGMLDEESLTVCEDGCRNKLHHHCMSIWAEECRNRREP
871-874   TSTSSSENSIKDEEEQMCPICLLGMLDEESLTVCEDGCRNKLHHHCMSIWAEECRNRREP
Active   -----

MEKK      LICPLCRSKWRSHDFYSHELSSPVESPASLRAVQQPSSPQQPVAGSQRRNQESSFNLTHF
871      LICPLCRSKWRSHDFYSHELSSPVESPASLRAVQQPSSPQQPVAGSQRRNQESSFNLTHF
871-874   LICPLCRSKWRSHDFYSHELSSPVESPASLRAVQQPSSPQQPVAGSQRRNQESSFNLTHF
Active   -----

MEKK      GTQQIPSAYKDLAEPWIQVFGMELVGCLFSRNWNVREMA LRRLSHDVSGALLANGESTG
871      GTQQIPSAYKDLAEPWIQVFGMELVGCLFSRNWNVREMA LRRLSHDVSGALLANGESTG
871-874   GTQQIPSAYKDLAEPWIQVFGMELVGCLFSRNWNVREMA LRRLSHDVSGALLANGESTG
Active   -----

MEKK      NSGGGSGGSLSAGAASGSSQPSISGDVVEACCSVLSIVCADPVYKVYVAALKTLRAMLVY
871      NSGGGSGGSLSAGAASGSSQPSISGDVVEACCSVLSIVCADPVYKVYVAALKTLRAMLVY
871-874   NSGGGSGGSLSAGAASGSSQPSISGDVVEACCSVLSIVCADPVYKVYVAALKTLRAMLVY

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Active

MEKK TPCHSLAERIKLQRLLRPVVDITLVKCADANSRTSQLSISTVLELCKGQAGELAVGREIL
 871 TPCHSLAERIKLQRLLRPVVDITLVKCADANSRTSQLSISTVLELCKGQAGELAVGREIL
 871-874 TPCHSLAERIKLQRLLRPVVDITLVKCADANSRTSQLSISTVLELCKGQAGELAVGREIL
 Active -----

MEKK KAGSIGVGGVDYVLSICILGNQAESNNWQELLGRLCLIDRLLLEFPAEFYPHIVSTDVSQA
 871 KAGSIGVGGVDYVLSICILGNQAESNNWQELLGRLCLIDRLLLEFPAEFYPHIVSTDVSQA
 871-874 KAGSIGVGGVDYVLSICILGNQAESNNWQELLGRLCLIDRLLLEFPAEFYPHIVSTDVSQA
 Active -----

MEKK EPVEIRYKKLLSLLTFALQSIDNSHSMVGKLSRRIYLSSARMVTAVPAVFSKLVTMLNAS
 871 EPVEIRYKKLLSLLTFALQSIDNSHSMVGKLSRRIYLSSARMVTAVPAVFSKLVTMLNAS
 871-874 EPVEIRYKKLLSLLTFALQSIDNSHSMVGKLSRRIYLSSARMVTAVPAVFSKLVTMLNAS
 Active -----

MEKK GSTHFTRMRRRLMAIADEVEIAEVIQLGVEDTVDGHQDSLQAVAPTSCLENSSSLEHTVHR
 871 GSTHFTRMRRRLMAIADEVEIAEVIQLGVEATVDGHQDSLQAVAPTSCLENSSSLEHTVHR
 871-874 GSTHFTRMRRRLMAIADEVEIAEVIQLGVEAAAAGHQDSLQAVAPTSCLENSSSLEHTVHR
 Active -----GHQDSLQAVAPTSCLENSSSLEHTVHR

MEKK EKTGKGLSATRLSASSEDISDRLAGVSVGLPSSTTTEQPKPAVQTKGRPHSQCLNSSPLS
 871 EKTGKGLSATRLSASSEDISDRLAGVSVGLPSSTTTEQPKPAVQTKGRPHSQCLNSSPLS
 871-874 EKTGKGLSATRLSASSEDISDRLAGVSVGLPSSTTTEQPKPAVQTKGRPHSQCLNSSPLS
 Active EKTGKGLSATRLSASSEDISDRLAGVSVGLPSSTTTEQPKPAVQTKGRPHSQCLNSSPLS

MEKK HAQLMFPAPSAPCSSAPSVDPISKHRPQAFVPCKIPASAPQTRKFSLQFQRNCSEHRDS
 871 HAQLMFPAPSAPCSSAPSVDPISKHRPQAFVPCKIPASAPQTRKFSLQFQRNCSEHRDS
 871-874 HAQLMFPAPSAPCSSAPSVDPISKHRPQAFVPCKIPASAPQTRKFSLQFQRNCSEHRDS
 Active HAQLMFPAPSAPCSSAPSVDPISKHRPQAFVPCKIPASAPQTRKFSLQFQRNCSEHRDS

MEKK DQLSPVFTQSRPPSSNIHRPKPSRPVPGSTSKLGDATKSSMTLDLGSASRCDDSFSGGGG
 871 DQLSPVFTQSRPPSSNIHRPKPSRPVPGSTSKLGDATKSSMTLDLGSASRCDDSFSGGGG
 871-874 DQLSPVFTQSRPPSSNIHRPKPSRPVPGSTSKLGDATKSSMTLDLGSASRCDDSFSGGGG
 Active DQLSPVFTQSRPPSSNIHRPKPSRPVPGSTSKLGDATKSSMTLDLGSASRCDDSFSGGGG

MEKK NSGNAVIPSDETVFTPVEDKCRLDVNTELNSSIEDLLEASMPSSDTTVTFKSEVAVLSPE
 871 NSGNAVIPSDETVFTPVEDKCRLDVNTELNSSIEDLLEASMPSSDTTVTFKSEVAVLSPE
 871-874 NSGNAVIPSDETVFTPVEDKCRLDVNTELNSSIEDLLEASMPSSDTTVTFKSEVAVLSPE
 Active NSGNAVIPSDETVFTPVEDKCRLDVNTELNSSIEDLLEASMPSSDTTVTFKSEVAVLSPE

MEKK KAENDDTYKDDVNHNNQCKEKMEEEEEALAIAMAMSASQDALPIVPQLQVENGEDI III
 871 KAENDDTYKDDVNHNNQCKEKMEEEEEALAIAMAMSASQDALPIVPQLQVENGEDI III
 871-874 KAENDDTYKDDVNHNNQCKEKMEEEEEALAIAMAMSASQDALPIVPQLQVENGEDI III
 Active KAENDDTYKDDVNHNNQCKEKMEEEEEALAIAMAMSASQDALPIVPQLQVENGEDI III

MEKK QQDTPETLPGHTKAKQPYREDAEWLKGQQIGLGAFFSSCYQAQDVGTGTLMAVKQVTTYVRN
 871 QQDTPETLPGHTKAKQPYREDAEWLKGQQIGLGAFFSSCYQAQDVGTGTLMAVKQVTTYVRN
 871-874 QQDTPETLPGHTKAKQPYREDAEWLKGQQIGLGAFFSSCYQAQDVGTGTLMAVKQVTTYVRN
 Active QQDTPETLPGHTKAKQPYREDAEWLKGQQIGLGAFFSSCYQAQDVGTGTLMAVKQVTTYVRN

MEKK TSSEQEEVVEALREEIRMMGHLNHPNIIIRMLGATCEKSNNYLFIEWMAGGSVAHLLSKYG
 871 TSSEQEEVVEALREEIRMMGHLNHPNIIIRMLGATCEKSNNYLFIEWMAGGSVAHLLSKYG
 871-874 TSSEQEEVVEALREEIRMMGHLNHPNIIIRMLGATCEKSNNYLFIEWMAGGSVAHLLSKYG
 Active TSSEQEEVVEALREEIRMMGHLNHPNIIIRMLGATCEKSNNYLFIEWMAGGSVAHLLSKYG

MEKK
871
871-874
Active

AFKESVVINYTEQLLRGLSYLHENQIIHRDVKGANLLIDSTGQRLRIADFGAAARLASKG
AFKESVVINYTEQLLRGLSYLHENQIIHRDVKGANLLIDSTGQRLRIADFGAAARLASKG
AFKESVVINYTEQLLRGLSYLHENQIIHRDVKGANLLIDSTGQRLRIADFGAAARLASKG

MEKK
871
871-874
Active

TGAGEFQGQLLGTIAFMAPEVLRGQQYGRSCDVWSVGCAIEMACAKPPWNAEKHSNHLA
TGAGEFQGQLLGTIAFMAPEVLRGQQYGRSCDVWSVGCAIEMACAKPPWNAEKHSNHLA
TGAGEFQGQLLGTIAFMAPEVLRGQQYGRSCDVWSVGCAIEMACAKPPWNAEKHSNHLA
TGAGEFQGQLLGTIAFMAPEVLRGQQYGRSCDVWSVGCAIEMACAKPPWNAEKHSNHLA

MEKK
871
871-874
Active

LIFKIASATTAPSIPSHLSPGLRDVAVRCLELQPQDRPPSRELLKHPVFRTTW
LIFKIASATTAPSIPSHLSPGLRDVAVRCLELQPQDRPPSRELLKHPVFRTTW
LIFKIASATTAPSIPSHLSPGLRDVAVRCLELQPQDRPPSRELLKHPVFRTTW
LIFKIASATTAPSIPSHLSPGLRDVAVRCLELQPQDRPPSRELLKHPVFRTTW
